UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/915,615	07/26/2001	Marta Gomez-Chiarri	5408	6818

55740 7590 07/20/2009

GAUTHIER & CONNORS, LLP
225 FRANKLIN STREET
SUITE 2300
BOSTON, MA 02110

EXAMINER	
GRASER, JENNIFER E	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
07/20/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/915,615	GOMEZ-CHIARRI ET AL.	
	Examiner	Art Unit	
	Jennifer E. Graser	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *7 and 8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 9-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Examiner of Record has changed from 'Examiner David Lambertson' to 'Examiner Jennifer Graser' of Art Unit 1645.

The above-cited application became abandoned for failure to reply in a timely manner to the non-final Office action mailed September 16, 2004, which set a shortened statutory period for reply of three (3) months from its mailing date. No extension of time pursuant to 37 CFR 1.136(a) was obtained within the allowable period. Accordingly, the application became abandoned on December 17, 2004. A Notice of Abandonment was mailed on August 9, 2005. A petition under 37 CFR 1.137(b) was first filed on February 8, 2007, and dismissed by a decision mailed October 26, 2007. There was a two and half year delay before Applicants filed a response/petition.

The amendment filed February 8, 2007, is noted.

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 1-6 and 9-17 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 11-20 of U.S. Patent No. 6,913,757. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patented claims are drawn to methods of inducing an immune response in an animal which can be fish, bivalves and crustaceans, while the instant claims limit the animal to fish. Additionally, the patented claims are a species of the instantly recited Genus claims as they specify that the bacteria used in the methods is a live, attenuated V.anguillarum which comprises a mugA gene comprising nucleotides 1218-2610 of SEQ ID NO:1 that renders said strain incapable of expressing a functional mugA protein (the strain is transformed with a plasmids comprising DNA of interest encoding at least one protein antigen from a pathogen). The immersion of fish in a solution comprising the transformed V.anguillarum strain is encompassed in 'administering the transformed strain to the animal'. Accordingly, the claims at not patentably distinct from one another.

Specification

3. The incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. See page 26, lines 1-8. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment

must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f).

The disclosure is objected to because of the following informalities: the US serial number recited on page 26, line 5, is missing. Applicant should amend the specification accordingly.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-6 and 9-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 recites the limitation "the dead, whole celled bacterium" in line 3. There is insufficient antecedent basis for this limitation in the claim because the preceding lines solely recite transforming 'a bacterium' and do not recite 'dead/killed or whole celled'.

Claim 11 is also vague and indefinite due to the phrase 'such that the DNA is delivered to the fish' by this does not convey whether this is a gene therapy type approach as it implies but instead it actually appears that the DNA is not being delivered

to the host, rather the recombinant bacterium is being delivered such that it will express the protein in the host. This is different from a gene intergration into the host per se. Clarification and/or correction is requested.

Claims 1-3, 6, 9-11 and 17 are drawn to a method of inducing an immune response using in a fish using an undefined product. The claims only recite a transformed bacterium with any vector comprising any DNA encoding any protein antigen. This is not sufficient to satisfy the Statute's requirement of adequately describing and setting forth the inventive concept. The claim should provide any structural properties, such as the nucleic acid sequence or the amino acid sequence it encodes, which would allow for one to identify transformed host cell which is the novel invention. The mere recitation of a name does not adequately define the claimed protein.

Claims 4 and 12 are vague and indefinite because it the mere recitation of a name, i.e., genes coding for the G proteins of the Viral Hemorrhagic Septiceamia Virus, genes coding for the G proteins from the infectious Hematpoietic Necrosis virus, *p57* gene, *empa* gene and *aspa* gene, etc., to describe the mutant gene contained in the dead, attenuated strain is not sufficient to satisfy the Staute's requirement of adequately describing and setting forth the inventive concept. It is unclear what structures are represented by these names. The specification does not provide a description of this gene's function or it's product's function. The claims should provide any structural properties, such as the nucleotide sequence genes, which would allow for one to identify the mutant without ambiguity. The mere recitation of a name does not

adequately define the claimed strain. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed.

Claims 9 and 17 are vague and indefinite because it the mere recitation of a name, i.e., mugA, to describe the mutant gene contained in the dead, attenuated strain is not sufficient to satisfy the Staute's requirement of adequately describing and setting forth the inventive concept. It is unclear what is represented by the name "mugA". The specification does not provide a description of this gene's function or it's product's function. It is unclear how one would be able to identify this mutant without knowing the gene's nucleotide sequence or the location of its mutation. The claim should provide any structural properties, such as the nucleotide sequence of the mugA gene, which would allow for one to identify the mutant without ambiguity. The mere recitation of a name does not adequately define the claimed strain. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed. The claim should be amended to comprise the nucleotide sequence of mugA.

Claim Rejections - 35 USC § 112-Enablement

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-6 and 9-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for a method of inducing an immune response in a fish comprising administering(immersing the fish in a solution) comprising 'a live, attenuated strain of *V.anguillarum* which comprises: a *mugA* gene comprising nucleotides 1218-2610 of SEQ ID NO:1 (this sequence must be properly incorporated from reference from the application recited on page 26 and given an appropriate sequence identifier for the instant application) , the strain having a mutation located within nucleotides 1218-2610 of SEQ ID NO:1 that renders the strain incapable of expressing a functional *mugA* protein" [this material when properly incorporated by reference; page 26], further, the specification only teaches the use of *E.coli or V.anguillarum* in the methods (e.g., not any transformed bacteria), does not reasonably provide enablement for "a method of inducing an immune response in a fish through the use of *any* bacterium transformed with *any* eukaryotic vector comprising *any* DNA of interest of any protein or a method of inducing an immune response in a fish which uses a live, attenuated strain of *V.anguillarum* which comprises a mutated *mugA* gene, the strain characterized in that it is incapable of expressing a functional *mugA* protein", nor is the scope enabled for claims 4 and 12 which recite genes for which there is no description of their nucleic acid sequence in the specification. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these

claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the

The specification is silent as to the exact function of the *mugA* gene and its gene products. However, instant specification (as incorporated by reference on page 26) teaches that a live, attenuated mutant designated M93Sm D contains an insertion in the *mugA* gene represented by SEQ ID NO:1 which renders the strain avirulent and able to protect fish against wild-type *Vibrio anguillarum*. The mutant strain disclosed in the instant specification contains an insertion in the *mugA* gene which is represented by SEQ ID NO:1. However, it is suggested that the *mugA* gene products may enable the bacterium to better grow in mucus. The claimed mutant was selected on its inability to grow in mucus and its ability to protect against wild-type *Vibrio anguillarum* while not harming the host. The sequence set forth in SEQ ID NO:1 is critical to the invention in that it is needed in order to develop mutants which are avirulent and cannot grow in mucus and which can protect the subject against wild-type *Vibrio anguillarum* . Without the sequence set forth in SEQ ID NO:1, it would take undue experimentation for one of skill in the art to make a mutant with the properties specific to M93Sm D and which would have the ability to protect against wild-type *Vibrio anguillarum*. The vaccine art is highly unpredictable and it would take undue experimentation to produce a mutant with the properties of M93Sm D by mutating any other gene than SEQ ID NO:1. The method of mutation, i.e., deletion or insertion, is not critical as long as the mutant possesses the desired properties because these techniques were routine in the art at the time the invention was made. However, the gene to be mutated is a critical element

and must be claimed. The specification does not identify any other *mugA* gene. As stated above, while the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The present invention is not enabled for mutants with mutations in any other gene except the one set forth in SEQ ID NO:1.

The instant specification fails to teach the nucleotide sequences of the genes recited in instant claims 4 and 12, e.g., *p57* gene from Renibacterium salmoninarum, *empa* gene from Vibrio anguillarum, *aspa* gene from Aeromonas salmonicida, *omp48* genes from Aeromonas veronii, *omp38* genes from Aeromonas veronii genes coding for the G proteins from the Infectious Hematopoietic Necrosis Virus and genes coding for the G proteins the Viral Hemorrhagic Septiceamia Virus. Accordingly, it would take undue experimentation for one skilled in the art to be able to create an expression vector with this non-disclosed DNA in order to transform a bacteria to effect the expression of the antigen it encodes in fish. Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001 clearly states: "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried

out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention."

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification coupled with information known in the art without undue experimentation (United States v. Telectronics., 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based upon a single factor but rather is a conclusion reached by weighing many factors. These factors were outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988), and the most relevant factors are indicated below:

Nature of the invention. The nature of the invention is a method of inducing an immune response in a fish through the transfer of a DNA vaccine (carried on a vector/plasmid) into a target fish organism via a killed bacterial cell. In order to practice the invention, the skilled artisan requires a plasmid DNA sequence that is capable of replicating in the bacterial cell, and which can express the antigenic protein in the target fish upon its transfer such that the protein can induce an immune response in the host. A teaching of the nucleic acid sequence, e.g., specific genetic material, to be used in the claimed methods is required.

Breadth of the claims. The claims are broad in terms of the bacterial cell that can be used to induce the antigenic response in a fish cell. This is because the types of

bacteria that are both can be transformed with an appropriate DNA vector (as set forth above) are narrower in scope than any possible bacteria, as set forth in the claims. The claims also recite the use of DNA of interest for which no nucleotide sequence is provided for in the instant specification.

State of the art. At the time of filing, many techniques for inducing an immune response in fish were known in the art; these include direct injection of naked DNA into a target fish, immersion of the target fish in a solution of naked plasmid DNA (i.e., not in a bacterial cell), and introduction of purified antigenic protein to the target fish. The state of the art as it generally regards bacterial transfer of a DNA vector to a target cells indicates that a particular limiting aspect is the ability of the bacteria to invade the target cell (see for example Grillot-Courvalin et al., Nat. Biotech. 16:862-866, 1998; see entire document, especially the Abstract). However, the state of the art at the time of filing was silent as to which fish-invasive bacteria could be used to transfer a particular DNA vector to a fish, such that an immune response is induced. Thus, the skilled artisan would need to consult the instant specification as to which invasive bacteria could successfully transfer a particular DNA vector to a fish, and what vectors could be used to acquire the invasive bacteria to be used therein. Additionally, the genetic material to be used would also need to be sufficiently recited in the specification, e.g., actual nucleic acid sequences, versus just the name of a gene.

Number of working examples and Guidance provided by applicant. The instant specification provides working examples regarding two distinct bacteria that are both invasive to fish and which can carry DNA vectors capable of replicating in the bacterial

cells and expressing the antigenic protein, thereby inducing an immune response in the target fish. These two bacteria are E. coli and V. anguillarum. There is little guidance as to what additional bacteria could replicate and transfer a DNA vector that would produce an antigenic protein in a fish cell and cause the fish to mount an appropriate immune resposne. Thus, it is unclear how the skilled artisan would use bacteria other than E. coli and V. anguillarum to use the claimed invention.

Unpredictability of the art and Amount of experimentation required. The invention as claimed would require an undue amount of unpredictable trial and error experimentation in order to use the method across its full scope. While the skilled artisan would understand the vectors that could be used in E. coli and V. anguillarum, the skilled artisan would need to empirically determine (a) what other bacteria would have an invasive characteristic towards fish, such that a DNA vector could be transferred therein and (b) what vectors could be used in these bacterium to successfully cause the expression of an antigenic protein in the target fish. Because it is not immediately clear from either the instant specification or the prior art as to which bacteria and respective vectors will have this invasive and immune inducing capacity, the skilled artisan could not use the invention across its broadly claimed scope. The instant specification fails to teach the nucleotide sequences of the genes recited in instant claims 4 and 12, e.g., *p57* gene from Renibacterium salmoninarum, *empa* gene from Vibrio anguillarum, *aspa* gene from Aeromonas salmonicida, *omp48* genes from Aeromonas veronii, *omp38* genes from Aeromonas veronii genes coding for the G proteins from the Infectious Hematopoietic Necrosis Virus and genes coding for the G

proteins the Viral Hemorrhagic Septiceamia Virus. Accordingly, it would take undue experimentation for one skilled in the art to be able to create an expression vector with this non-disclosed DNA in order to transform a bacteria to effect the expression of the antigen it encodes in fish.

NOTE: it is unclear why the previous Examiner rejoined the methods recited in claims 11-17 (Group IV) to the elected Group since the method recited therein is not the same, e.g., it is drawn merely to a method for the delivery of DNA in a fish and includes nothing about raising/inducing an immune response (as in Groups I and III), nor is the search for it coextensive with the Elected Group I and rejoined Group III.

There are no working examples in the instant specification to guide the skilled artisan in practicing the claimed method. Only the specific V.anguillarum or E.coli hosts are taught. There are no other examples of delivery of any other therapeutic agent present in the specification. The state of the art for gene therapy as discussed by Vile et al (Gene Therapy, Vol. 7, pp. 2-8, 2000) is unpredictable. Vile et al teach that the problems in which gene therapy for cancer will take into the next millennium focus far less on the choice of therapeutic gene(s) to be used than on the means of delivering them. Vile et al teach that there is already a battery of genes that we know are very effective in killing cells and if these genes can be expressed at the right site and at appropriate levels therapy may be occur (page 2). However, until the perfect vector is developed, the choice of gene will remain crucially important in order to compensate for the deficiencies of the vectors we currently have available (page 2, 1st paragraph, left column). Vile et al. teach that whatever its mechanism, no single genes can be a

serious contender unless it has a demonstrable bystander effect (page 2, right column) and the requirement for such a bystander effect stems directly from the poor delivery efficiency provided by current vectors (page 2, right column). Vile et al teach that a genuine ability to target delivery systems to tumor cells distributed widely throughout the body of a patient would simultaneously increase real titers and efficacy. Vile et al teach that in truth, no such systemically targeted vectors exist yet. Vile et al teach that injection of vectors into the bloodstream for the treatment of cancer requires not only that the vectors be targeted (to infect only tumor cells) but also that they by protected (from degradation, sequestration or immune attack) for 10ng periods of time so that they can reach the appropriate sites for infection. Moreover, having reached such sites, the vectors must be able to penetrate into the tumor from the bloodstream before carrying out their targeted infection (page 4, bottom left column and top right column). In addition, Rochlitz C. F. (Swiss Medicine Weekly, 131:4-9, 2001) teaches that none of the more than one hundred Clinical studies performed so far had formally proven efficacy of the approach (gene therapy) in any disease. Rochilitz teaches that although anecdotal reports of tumor responses are becoming more frequent in several human malignancies, the situation has not changed dramatically." (see page 8, bottom of page). Rochlitz teaches that the main problems are still the lack of vectors with high transduction efficiency in vivo, the low tumor specificity of available systems, and our incomplete knowledge of molecular tumor pathology" (pages 8-9).

Thus, as taught above, the state of the art regarding gene therapy is considered highly unpredictable. Furthermore, it would take one skilled in the art

an undue amount of experimentation to determine what route of administration (e.g. intravenous, dermal, nasal, rectal, vaginal, inhalation, or topical administration) would result in a therapeutic response using a recombinant bacterium comprising the nucleic acid encoding the antigen. The state of the art regarding the route of administration for gene therapy as exemplified by Verma et al, (Nature, Vol. 389, No. 6648, pages 239-242, 1997), indicates that factors including the nature of the diseases and/or disorders, the nature of a DNA and/or target tissue, and a delivery system and/or amounts of the DNA complexes employed in the delivery system that would generate a therapeutic effect in vivo must be considered for any gene therapy method to be successful (page 238, columns 1 and 2). Therefore, the skilled artisan at the time the invention was made recognized the lack of predictability of the nature of the art and state of the prior art to which the instant invention pertains. Also, such disclosures clearly indicate that the amount of direction or guidance presented in the specification is limited, and would not permit a person skilled in the art to use the invention without undue experimentation at the time the invention was made.

In view of the lack of predictability of the art to which the invention pertains, the lack of established clinical protocols for effective gene therapies, and for the lack of enabling description for the delivery of any other therapeutic agents to the cells, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed

methods are effective for treating a genetic disorder, or any other condition or disease in a patient.

Given the lack of guidance contained in the specification regarding acceptable amino acid substitutions, one of skill in the art could not make or use the broadly claimed invention without undue experimentation.

Response to Applicant's previous arguments (2/8/07):

Applicants argue that they have shown that immersion in killed and live E.coli, which does not have the ability to invade fish, by immersion results in the delivery of DNA to several fish tissues, including liver and kidney. This has been fully and carefully considered but is not sufficient to overcome the rejection as the specification fails to teach any bacteria other than E.coli or V.anguillarum or the specific nucleic acid material capable of mounting an appropriate immune response in fish. See above.

Claim Rejections - 35 USC э 112-Written Description

8. Claims 1-6 and 9-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In 1999, the United States Patent and Trademark Office ("USPTO") published training materials regarding the examination of patent applications under the written description requirement of 35 U.S.C. § 112, first paragraph. (See http ://www.uspto. gov/web/offices/pac/writtende sc.pdf). Since that time, the case

law and technology have developed in such a way as to necessitate a revision of the 1999 training materials. Consequently, this 2008 revision was created to supersede and replace the 1999 training materials. To the extent that any conflict exists between the 1999 training materials and the present materials, the present materials control. The claims have been evaluated with regard to written description based on the Written Description Guidelines and Training Materials published in 2008/

To fulfill the written description requirements set forth under 35 USC § 112, first paragraph, the specification must describe at least a substantial number of the members of the claimed genus, or alternatively describe a representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that Applicant has possession the claimed invention. Applicants have not described the genus of claimed nucleotides such that the specification might reasonably convey to the skilled artisan that Applicants had possession of the claimed invention at the time the application was filed.
The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed. See Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991).

Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, "'Written Description" Requirement (66 FR 1099-1111, January 5,2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (Id. at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was

filed. The Guidelines further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus'" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus The written description in this case only sets forth the *mugA* gene contained in SEQ ID NO:1 and therefore the written description is not commensurate in scope with the claims drawn to mutants comprising a mutation in *any* mugA gene other than the one set forth in SEQ ID NO:1. The instant specification fails to teach the nucleotide sequences of the genes recited in instant claims 4 and 12, e.g., *p57* gene from Renibacterium salmoninarum, *empa* gene from Vibrio anguillarum, *aspa* gene from Aeromonas salmonicida, *omp48* genes from Aeromonas veronii, *omp38* genes from Aeromonas veronii genes coding for the G proteins from the Infectious Hematopoietic Necrosis Virus and genes coding for the G proteins the Viral Hemorrhagic Septiceamia Virus and, therefore, lacks written description for these recombinant bacteria/expression vectors.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Reiger et al (Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlay, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome..... and differing from other alleles of that locus at one or more mutational sites (page 17). Thus, the structure of naturally occurring allelic sequences are not defined. With the exception of SEQ ID NO:1(this sequence must be properly incorporated from reference from the application recited on page 26 and given an appropriate sequence identifier for the instant application), the skilled artisan cannot envision the detailed structure of the encompassed polynucleotides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Lts., 18 USPQ2d 1016.

Furthermore, In The Reagents of the University of California v. Eli Lilly (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a

nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Therefore, the full breadth of the claims meets the written description provisions of 35 USC 112, first paragraph.

Status of Claims:

The last Office Action was mailed on 9/16/04. There was a two and half year delay before Applicants filed a response/petition. In the interim, guidelines have changed for 35 USC 112, first paragraph, Written Description.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Remsen. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is 571-273-8300 which is able to receive transmissions 24 hours/day, 7 days/week.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (571) 272-0858. The examiner can normally be reached on Monday-Thursday from 8:00 AM-6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi, can be reached on (571) 272-0956.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0500.

/Jennifer E. Graser/
Primary Examiner, Art Unit 1645

7/15/09